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ZYTIGA® (abiraterone acetate) Plus Prednisone Approved for Treatment of Earlier Form of Metastatic Prostate Cancer

New indication for ZYTIGA® in combination with prednisone provides treatment option for patients with metastatic high-risk castration-sensitive prostate cancer

Findings from pivotal Phase 3 LATITUDE clinical trial data demonstrated statistically significant and clinically meaningful improvements in patients

HORSHAM, PA, Feburary 8, 2018 – The Janssen Pharmaceutical Companies of Johnson & Johnson today announced that the U.S. Food and Drug Administration (FDA) has approved a new indication for ZYTIGA® (abiraterone acetate) in combination with prednisone for the treatment of patients with metastatic high-risk castration-sensitive prostate cancer (CSPC). The approval is based on Phase 3 data from the pivotal LATITUDE clinical trial, which found that in patients with metastatic high-risk CSPC, ZYTIGA® in combination with prednisone reduced the risk of death by 38 percent compared to placebos.

"LATITUDE was a large global trial which produced impressive and clinically significant results in overall survival," said Karim Fizazi, M.D., Ph.D., Principal Investigator and Head of the Medical Oncology Department at Institute Gustave Roussy, Villejuif, France. "With today's approval, abiraterone acetate plus prednisone could become a standard of care for patients with metastatic high-risk castration-sensitive prostate cancer."

"Today's approval marks an important step in addressing the unmet needs of patients with metastatic high-risk castration-sensitive prostate cancer by providing an option that has demonstrated improvement in overall survival," said Andree Amelsberg, M.D., Vice President of Oncology Medical Affairs at Janssen Biotech, Inc., part of the Janssen Pharmaceutical Companies of Johnson & Johnson. "This milestone is an exciting turning point for researchers and clinicians, and

most importantly, for patients suffering from this disease and their families who now have an important additional therapeutic option."

LATITUDE was a multinational, multicenter, randomized, double-blind, placebo-controlled clinical trial that examined the use of ZYTIGA® 1,000 mg once daily in combination with prednisone 5 mg once daily, compared to placebos (N=1,199) in patients with newly diagnosed, metastatic high-risk CSPC, who had not received prior cytotoxic chemotherapy. All the patients received a gonadotropin-releasing hormone (GnRH) analog or had prior bilateral orchiectomy. The study data were presented at the plenary session of the 2017 American Society of Clinical Oncology (ASCO) Annual Meeting in Chicago, and simultaneously published in *The New England Journal of Medicine*.[1] The study showed ZYTIGA® in combination with prednisone reduced the risk of death by 38 percent compared to placebos (median OS not estimable vs. 34.7 months, respectively; hazard ratio (HR)=0.62; 95% confidence interval (CI): [0.51, 0.76], p<0.0001). Additional data demonstrated statistically significant delay in time to initiation of chemotherapy for patients in the ZYTIGA® arm compared to those in the placebo arm (median time to initiation of chemotherapy not reached vs. 38.9 months, respectively; HR=0.44; 95% CI: [0.35, 0.56], p < 0.0001).

The most common adverse reactions (≥10%) that occurred more commonly (>2%) in the ZYTIGA® arm from an analysis of pooled safety data were fatigue, arthralgia, hypertension, nausea, edema, hypokalemia, hot flush, diarrhea, vomiting, upper respiratory infection, cough and headache.

On November 20, 2017, the European Commission (EC) granted approval to broaden the marketing authorization for ZYTIGA® in combination with prednisone or prednisolone to include newly-diagnosed high-risk metastatic hormone-sensitive prostate cancer (HSPC). Similar submissions have been made in Japan, Canada, Mexico, Switzerland, Singapore, and the Philippines, and approved in Brazil and Taiwan. If approved, these submissions will broaden the use of ZYTIGA® in combination with prednisone or prednisolone to include an earlier stage of prostate cancer than its current indications.

Metastatic prostate cancer is cancer that has spread to another part of the body.[2] Metastatic castration-sensitive prostate cancer (CSPC), also referred to as metastatic hormone-sensitive prostate cancer (HSPC) in literature, refers to prostate cancer that still responds to testosterone suppression therapy.[2] Patients with newly-diagnosed metastatic disease and high-risk disease characteristics tend to have a poorer prognosis.[3]

About the LATITUDE Clinical Trial[4]

The Phase 3, multinational, multicenter, randomized, double-blind, placebo-controlled LATITUDE study enrolled 1,199 patients with newly diagnosed metastatic, high-risk castration-sensitive prostate cancer (CSPC), who had not received prior cytotoxic chemotherapy. The study was conducted at 235 sites in 34 countries in Europe, Asia-Pacific, Latin America, and Canada. A total number of 597 patients were randomized to receive ZYTIGA® plus prednisone, while 602 patients were randomized to receive placebo. All patients received a gonadotropin-releasing hormone (GnRH) analog or had prior bilateral orchiectomy. High-risk disease was defined as having at least two of three risk factors at baseline: a total Gleason score of ≥8, presence of ≥3 lesions on bone scan, and evidence of measurable visceral metastases. Patients with significant cardiac, adrenal, or hepatic dysfunction were excluded. The median duration of treatment with ZYTIGA® and prednisone was 24 months.

About ZYTIGA®

ZYTIGA® (abiraterone acetate) in combination with prednisone is indicated for the treatment of patients

- with metastatic castration-resistant prostate cancer (CRPC)
- with metastatic high-risk castration-sensitive prostate cancer (CSPC)

Since its first approval in the U.S. in 2011, ZYTIGA® has been approved in combination with prednisone or prednisolone, in 105 countries. More than 330,000 patients worldwide, including 113,000 in the U.S., have received treatment with it, and it was the number one prescribed oral medication in the U.S. for patients with metastatic CRPC in 2016.

For more information about ZYTIGA®, visit www.ZYTIGA.com.

IMPORTANT SAFETY INFORMATION

Contraindications - ZYTIGA® (abiraterone acetate) can cause fetal harm and potential loss of pregnancy.

Hypertension, Hypokalemia and Fluid Retention Due to Mineralocorticoid Excess - ZYTIGA® may cause hypertension, hypokalemia, and fluid retention as a consequence of increased mineralocorticoid levels resulting from CYP17 inhibition *[see Clinical Pharmacology (12.1)]*. Monitor patients for hypertension, hypokalemia, and fluid retention at least once a month. Control hypertension and correct hypokalemia before and during treatment.

Closely monitor patients whose underlying medical conditions might be compromised by increases in blood pressure, hypokalemia or fluid retention, such as those with heart failure, recent myocardial

infarction, cardiovascular disease, or ventricular arrhythmia. The safety of ZYTIGA® in patients with left ventricular ejection fraction <50% or New York Heart Association (NYHA) Class III or IV heart failure (in COU-AA-301) or NYHA Class II to IV heart failure (in COU-AA-302 and LATITUDE) has not been established because these patients were excluded from these randomized clinical trials *[see Clinical Studies (14)]*.

Adrenocortical Insufficiency (AI) - AI was reported in patients receiving ZYTIGA® in combination with prednisone, after an interruption of daily steroids and/or with concurrent infection or stress. Monitor patients for symptoms and signs of AI if prednisone is stopped or withdrawn, if prednisone dose is reduced, or if the patient experiences unusual stress. Symptoms and signs of AI may be masked by adverse reactions associated with mineralocorticoid excess seen in patients treated with ZYTIGA®. Perform appropriate tests, if indicated, to confirm AI. Increased dosages of corticosteroids may be used before, during, and after stressful situations.

Hepatotoxicity - In postmarketing experience, there have been ZYTIGA®-associated severe hepatic toxicities, including fulminant hepatitis, acute liver failure and deaths. Measure serum transaminases alanine aminotransferase (ALT and AST) and bilirubin levels prior to starting treatment with ZYTIGA®, every two weeks for the first three months of treatment, and monthly thereafter. In patients with baseline moderate hepatic impairment receiving a reduced ZYTIGA® dose of 250 mg, measure ALT, AST, and bilirubin prior to the start of treatment, every week for the first month, every two weeks for the following two months of treatment and monthly thereafter. Promptly measure serum total bilirubin, AST, and ALT if clinical symptoms or signs suggestive of hepatotoxicity develop. Elevations of AST, ALT, or bilirubin from the patient's baseline should prompt more frequent monitoring. If at any time AST or ALT rise above five times the upper limit of normal (ULN) or the bilirubin rises above three times the ULN, interrupt ZYTIGA® treatment and closely monitor liver function. Re-treatment with ZYTIGA® at a reduced dose level may take place only after return of liver function tests to the patient's baseline or to AST and ALT less than or equal to 2.5X ULN and total bilirubin less than or equal to 1.5X ULN *[See Dosage and Administration (2.4)].*

Permanently discontinue ZYTIGA® for patients who develop a concurrent elevation of ALT greater than 3X ULN and total bilirubin greater than 2X ULN in the absence of biliary obstruction or other causes responsible for the concurrent elevation.

The safety of ZYTIGA® re-treatment of patients who develop AST or ALT greater than or equal to 20X ULN and/or bilirubin greater than or equal to 10X ULN is unknown.

Adverse Reactions - The most common adverse reactions (≥10%) are fatigue, arthralgia, hypertension, nausea, edema, hypokalemia, hot flush, diarrhea, vomiting, upper respiratory tract infection, cough, and headache.

The most common laboratory abnormalities (>20%) are anemia, elevated alkaline phosphatase, hypertriglyceridemia, lymphopenia, hypercholesterolemia, hyperglycemia and hypokalemia.

Drug Interactions - Based on *in vitro* data, ZYTIGA® is a substrate of CYP3A4. In a drug interaction trial, co-administration of rifampin, a strong CYP3A4 inducer, decreased exposure of abiraterone by 55%. Avoid concomitant strong CYP3A4 inducers during ZYTIGA® treatment. If a strong CYP3A4 inducer must be co-administered, increase the ZYTIGA® dosing frequency only during the co-administration period *[see Dosage and Administration (2.3)].* In a dedicated drug interaction trial, co-administration of ketoconazole, a strong inhibitor of CYP3A4, had no clinically meaningful effect on the pharmacokinetics of abiraterone.

ZYTIGA® is an inhibitor of the hepatic drug-metabolizing enzymes CYP2D6 and CYP2C8. Avoid co-administration with CYP2D6 substrates with a narrow therapeutic index. If alternative treatments cannot be used, consider a dose reduction of the CYP2D6 substrate drug. In a CYP2C8 drug interaction trial in healthy subjects, the AUC of pioglitazone, a CYP2C8 substrate, was increased by 46% when administered with a single dose of ZYTIGA®. Patients should be monitored closely for signs of toxicity related to a CYP2C8 substrate with a narrow therapeutic index if used concomitantly with ZYTIGA®.

Use in Specific Populations

- **Females and Males of Reproductive Potential: Advise males with female partners of reproductive potential to use effective contraception.**
- Do not use ZYTIGA® in patients with baseline severe hepatic impairment (Child-Pugh Class C).

About the Janssen Pharmaceutical Companies of Johnson & Johnson

At the Janssen Pharmaceutical Companies of Johnson & Johnson, we are working to create a world without disease. Transforming lives by finding new and better ways to prevent, intercept, treat and cure disease inspires us. We bring together the best minds and pursue the most promising science.

We are Janssen. We collaborate with the world for the health of everyone in it. Learn more at www.janssen.com. Follow us at www.twitter.com/JanssenGlobal and www.twitter.com/JanssenUS. Janssen Research & Development, LLC and Janssen Biotech, Inc. are part of the Janssen Pharmaceutical Companies of Johnson & Johnson.

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Cautions Concerning Forward-Looking Statements

This press release contains "forward-looking statements" as defined in the Private Securities Litigation Reform Act of 1995 regarding the impact of the approval of an expanded indication for ZYTIGA® (abiraterone acetate) and potential approvals and broadened use of ZYTIGA® in combination with prednisone or prednisolone. The reader is cautioned not to rely on these forward-looking statements. These statements are based on current expectations of future events. If underlying assumptions prove inaccurate or known or unknown risks or uncertainties materialize, actual results could vary materially from the expectations and projections of Janssen Biotech, Inc., any of the other Janssen Pharmaceutical Companies and/or Johnson & Johnson. Risks and uncertainties include, but are not limited to: challenges and uncertainties inherent in product research and development, including the uncertainty of clinical success and of obtaining regulatory approvals; uncertainty of commercial success; manufacturing difficulties and delays; competition, including technological advances, new products and patents attained by competitors; challenges to patents; product efficacy or safety concerns resulting in product recalls or regulatory action; changes in behavior and spending patterns of purchasers of health care products and services; changes to applicable laws and regulations, including global health care reforms; and trends toward health care cost containment. A further list and descriptions of these risks, uncertainties and other factors can be found in Johnson & Johnson's Annual Report on Form 10-K for the fiscal year ended January 1, 2017, including under "Item 1A. Risk Factors," its most recently filed Quarterly Report on Form 10-Q, including in the section captioned "Cautionary Note Regarding Forward-Looking Statements," and the company's subsequent filings with the Securities and Exchange Commission. Copies of these filings are available online at www.sec.gov, www.jnj.com or on request from Johnson & Johnson. Neither the Janssen Pharmaceutical Companies nor Johnson & Johnson undertakes to update any forward-looking statement as a result of new information or future events or developments.

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[1] Fizazi K., et al. Abiraterone plus Prednisone in Metastatic, Castration-Sensitive Prostate Cancer. New England Journal of Medicine. June 2017.

[2] American Society of Clinical Oncology. Prostate Cancer: Treatment Options. http://www.cancer.net/cancer-types/prostate-cancer/treatment-options. Accessed February 2018.

[3] Fizazi K., et al. LATITUDE: A phase III, double-blind, randomized trial of androgen deprivation therapy with abiraterone acetate plus prednisone or placebos in newly diagnosed high-risk metastatic hormone-naive prostate cancer. ASCO 2017. Abstract #LBA3.

[4] Clinical trials.gov. A Study of Abiraterone Acetate Plus Low-Dose Prednisone Plus Androgen Deprivation Therapy (ADT) Versus ADT Alone in Newly Diagnosed Participants With High-Risk, Metastatic Hormone-Naive Prostate Cancer (mHNPC). https://clinicaltrials.gov/ct2/show/NCT01715285. Accessed February 2018.